I. FORMAL MATTERS

A. Claim Status & Amendments

The Specification at page 17 has been amended to better clarify the Brief Description of the Drawings for Figures 2A and 2B. Support for this amendment can be found in the Specification, at least at page 17, lines 1-2 and in Figure 2 as originally filed. Accordingly, no new matter is believed to have been added by this amendment.

As correctly indicated in the Office Action Summary, claims 24-45 are presently pending in this application. The present amendment amends claims 24 and 25 to more clearly define the present invention. Support these amendments can be found, at least, in original claims 24 and 25. Accordingly, no new matter is believed to have been added by this amendment.

The present amendment also cancels claims 26-32 and 36-42 without prejudice or disclaimer to the subject matter recited therein. Applicants reserve the right to file a continuation or divisional application directed to any of the canceled subject matter.

Upon entry of the present Amendment and Reply, claims 24, 25, 33-35, 43-45 will be pending in this application.

B. Proposed Amendments to the Drawings

Pursuant to 37 C.F.R. § 1.121, Applicants hereby submit a copy of the originally filed Figure 2 with proposed amendments in red for approval by the Examiner. Applicants request approval of the proposed drawing changes. Upon approval by the Examiner, Applicants will submit a new Figure 2 reflecting the approved changes.

The proposed changes to Figure 2 more accurately reference the panels A and B as Figure 2A and Figure 2B. Support for these proposed amendment can be found in Figure 2 as originally filed. Accordingly, no new matter is believed to have been added by this amendment.

II. OBJECTIONS TO THE SPECIFICATION

A. Priority Data

The Specification has been objected for allegedly not containing a reference to the prior applications in the first sentence of the Specification. See August 12, 2002 Official Action, page 2. Applicants traverse this objection and respectfully note that this objection is in error. The Examiner's attention is drawn to the fact that the February 21, 2001 Transmittal Letter to the Patent & Trademark Office (a copy of which is attached herewith) included an amendment to the Specification to insert the priority data at page 1, line 1 of the Specification. Thus, Applicants respectfully request withdrawal of this objection.

B. Brief Description of the Drawings

The Specification has been objected to as allegedly failing to provide a description of panels A and B in Figure 2 in the Brief Description of the Drawings. See March 12, 2002 Official Action, page 2.

The present amendment hereby amends the Brief Description of the Drawings to more precisely reference panels A and B in Figure 2 as "Figure 2A" and "Figure 2B." Figure 2 has also been requested to be amended to more accurately reflect this reference to "Figure 2A" and "Figure 2B." A Request for Approval of Drawing Changes has been

filed concurrently herewith. Thus, Applicants respectfully request the withdrawal of this objection.

III. REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 24-45 stand rejected under 35 U.S.C. § 112, first paragraph, because the Specification is allegedly not enabled for the full scope of the claimed invention. See March 12, 2002 Official Action, pages 2-5.

At the outset, Applicants note that the full lack of enablement rejection has been modified to a scope of enablement rejection in view of the arguments set forth in the May 15, 2002 Amendment and Reply. Now, the Examiner believes that the Specification is enabling only for a method of treating multiple sclerosis wherein a nucleic acid encoding a beta-interferon comprising beta-interferon secretory signal is directly administered to muscle cells and a pharmaceutical composition thereof, wherein the nucleic acid is DNA or naked DNA, wherein the DNA is associated with a transfection-facilitating vehicle selected from the list of cationic lipids, cationic polymers, and polypeptides suitable for injection. The Examiner alleges that the Specification is not enabling for a method of treating any immune disease or any demyelinating disease or wherein the nucleic acid is administered by any other route.

Applicants respectfully traverse this rejection. Nonetheless, for the sole purpose of expediting prosecution and not to acquiesce to the Examiner's rejection, Applicants have amended the claims to the treatment of multiple sclerosis. Given that the present amendment renders the rejection moot, Applicants request the withdrawal of this rejection.

IV. REJECTIONS UNDER 35 U.S.C. § 102(b)

A. Triantaphyllopous (1999)

Claims 24-45 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Triantaphyllopous *et al.*, ARTHRITIS & RHEUMATISM, 42:90-99 (1999) ("Triantaphyllopous (1999)"). See March 12, 2002 Official Action, page 5.

According to the Examiner, Triantaphyllopous (1999) allegedly teaches a method for the introduction of INF-β expression vectors into EAE mice. This is a new grounds of rejection.

Applicants respectfully traverse this rejection. Nonetheless, for the sole purpose of expediting prosecution and not to acquiesce to the Examiner's rejection, Applicants have amended the claims to the treatment of multiple sclerosis via administrating naked DNA capable of expressing INF-β to a patient in need thereof. Triantaphyllopous (1999) fails to teach this element of the amended claims.

In particular, Triantaphyllopous (1999) fails to anticipate the claimed invention because the reference fails to disclose **each** and **every** element of the claimed invention. It is well established that to anticipate a claim, a single prior art reference must teach, either expressly or inherently, each and every element of the claimed invention. See M.P.E.P. § 2131; Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987); Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1379, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986).

In this regard, Triantaphyllopous (1999) fails to teach the treatment of **multiple sclerosis** via administrating **naked DNA** capable of expressing INF-β to a patient in need

thereof. Instead, Triantaphyllopous (1999) discloses the use of a plasmid comprising the IFN-β gene for the therapy of EAE in mice wherein said plasmid is associated with lipofecting and is injected intracranially. See Triantaphyllopous (1999), page 257, 1st full paragraph, 1st column. Applicants further note that Triantaphyllopous (1999) fails to suggest the claims as-amended either alone or in combination with the contemporary knowledge in the field at the time of Applicant's invention. Thus, as the cited reference fails to teach or suggest the as-amended claims, Applicants specifically request withdrawal of this rejection.

B. Triantaphyllopous (1998)

Claims 24-45 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Triantaphyllopous *et al.*, GENE THERAPY, 5:253-263 (1998) ("Triantaphyllopous (1998)"). See March 12, 2002 Official Action, page 5. This is a new grounds of rejection.

According to the Examiner, Triantaphyllopous (1998) teaches a method for the introduction of INF-β expression vectors into EAE mice. This is a new grounds of rejection.

Applicants respectfully traverse this rejection. Nonetheless, for the sole purpose of expediting prosecution and not to acquiesce to the Examiner's rejection, Applicants have amended the claims to the treatment of multiple sclerosis via administrating naked DNA capable of expressing INF-β to a patient in need thereof. Triantaphyllopous (1998) fails to teach this element of the amended claims.

In particular, Triantaphyllopous (1998) fails to anticipate the claimed invention because the reference fails to disclose **each** and **every** element of the claimed invention. It is well established that to anticipate a claim, a single prior art reference must teach, either expressly or inherently, each and every element of the claimed invention. See M.P.E.P. § 2131; Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987); Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1379, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986).

In this regard, Triantaphyllopous (1998) fails to teach the treatment of **multiple sclerosis** via administrating **naked DNA** capable of expressing INF-β to a patient in need thereof. Instead, Triantaphyllopous (1998) describes the intracranial injection of transfected fibroblasts expressing IFN-β to treat collagen induced arthritis in mice. See Triantaphyllopous (1998), Abstract. Applicants further note that Triantaphyllopous (1998) fails to suggest the claims as-amended either alone or in combination with the contemporary knowledge in the field at the time of Applicant's invention. Thus, as the cited reference fails to teach or suggest the as-amended claims, Applicants specifically request withdrawal of this rejection.

C. **Croxford**

Claims 24-45 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Croxford *et al.*, THE JOURNAL OF IMMUNOLOGY, 160:5181-5187 (1998). March 12, 2002 Official Action, page 5.

According to the Examiner, Croxford teaches a method for the introduction of INF-β expression vectors into EAE mice. This is a new grounds of rejection.

Applicants respectfully traverse this rejection. Nonetheless, for the sole purpose of expediting prosecution and not to acquiesce to the Examiner's rejection, Applicants have amended the claims to the treatment of multiple sclerosis via administrating naked DNA capable of expressing INF-β to a patient in need thereof. Croxford fails to teach or suggest this element of the amended claims.

In particular, Croxford fails to anticipate the claimed invention because the reference fails to disclose **each** and **every** element of the claimed invention. It is well established that to anticipate a claim, a single prior art reference must teach, either expressly or inherently, each and every element of the claimed invention. See M.P.E.P. § 2131; Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987); Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1379, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986).

In this regard, Croxford fails to teach the treatment of **multiple sclerosis** via administrating **naked DNA** capable of expressing beta-interferon to a patient in need thereof. Instead, Croxford describes the use of a plasmid comprising the gene coding for the IFN-β complexed with cationic liposomes for the treatment of EAE. See Croxford, Abstract.

To the extent that an attempt may be made to utilize Croxford in a subsequent obviousness rejection, Applicants note that Croxford also fails to suggest the claimed invention. In this regard, Croxford discloses that a single i.m. injection of 100 μg of cytokine DNA (*i.e.*, naked DNA) failed to ameliorate the disease severity or the onset of disease. Croxford, page 5182, 2nd column, last paragraph; page 5183, Table I. This same

failure is also observed when the DNA is injected intracranially. Croxford, page 5183, 2nd column, 1st full paragraph. Accordingly, one of ordinary skill in the art upon reading Croxford would not be motivated to use naked DNA coding for INF-β for the treatment of multiple sclerosis. Thus, as the cited reference fails to teach or suggest the as-amended claims, Applicants specifically request withdrawal of this rejection.

CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such action is earnestly solicited.

In the event that there are any questions relating to this Amendment and Reply, or to the application in general, the Examiner is invited to telephone the undersigned concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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ATTACHMENT TO AMENDMENT AND REPLY

Marked-up Copy of Specification

Paragraph at page 16, line 32 to page 17, line 2:

Figure 2: detection of human IFN-β in the blood of mice injected with pTG13102. Bars are man values +/- sem of 3 determinations (3 mice per group). White bars : after injection of plasmid prepared in NaCl 0.9%. Black bars : after administration of plasmid with adjuvants described in the text. [A] Figure 2A : injections in SCID mice. [B] Figure 2B : in immunocompetent C57BI/10 mice.

ATTACHMENT TO AMENDMENT AND REPLY

Marked-up Copy of Amended Claims 24 and 25

24. (Amended) A method for the treatment of [an immune disease] multiple sclerosis comprising administering an effective amount of [a nucleic acid] naked DNA capable of expressing beta-interferon to a patient in need of such treatment.

25. (Amended) A pharmaceutical composition for the treatment of [an immune disease] multiple sclerosis comprising an effective amount of [a nucleic acid] naked DNA capable of expressing beta-interferon and a pharmaceutically acceptable carrier therefor.